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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,350	02/15/2006	Yuzhang Wu	CCPT124975	5046

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EXAMINER

PENG, BO

ART UNIT	PAPER NUMBER
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1648

NOTIFICATION DATE	DELIVERY MODE
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09/02/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

efiling@cojk.com

Office Action Summary	Application No. 10/528,350	Applicant(s) WU ET AL.	
	Examiner BO PENG	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 June 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 5-74 is/are pending in the application.
- 4a) Of the above claim(s) 17-22,24-53,61 and 66-70 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 5-16,23,54-60,62-65 and 71-74 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This Office action is in response to the amendment filed on June 22, 2010. Claim 4 has been cancelled. Claims 1-3 and 5-74 are pending. Claims 42-53 and 70 have been withdrawn by Applicants. Claims 17-22, 24-41, 61 and 66-70 have been withdrawn. Claims 1-3, 5-16, 23, 54-60, 62-65 and 71-74 are examined in this Office action. The claims read on the elected species of a polypeptide sequence 1 of SEQ ID NO: 6, sequence 2 of SEQ ID NO: 23, sequence 3 of SEQ ID NO: 48, the linking peptide of AAA between sequences 1 and 2, and GGG between sequences 2 and 3, and CH₃(CH₂)₁₄CO- as modifying group (Claims 7-15), an injection formulation in Claim 59, and a lyophilized liposome dosage of Claim 72.

Claim Rejections - 35 USC 112, second paragraph

2. The following is a quotation of the second paragraph of 35 USC 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. **(Prior rejection-withdrawn)** The rejection of Claims 2 and 3 under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter of “variant sequences thereof”, **is withdrawn** in view of the amendment to the claims. The portion of the claims “variant sequences thereof” has been deleted. The rejection is therefore withdrawn.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 USC 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5. **(Prior rejection-withdrawn)** The rejection of Claims 1, 6 and 54-60 under 35

USC 102(a) as being anticipated by Madalinski K, *et al.* (Vaccine, 2001, 20(1-2):92-7), as

evidenced by Heermann, (*J Virol* 52 (1984), p. 396-493), Tam (PNAS 86:9084-9088, 1989) and

Roh (Virus Res. 73:17-26, 2001), **is withdrawn** in view of the amendment to the claims.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 USC 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. **(Prior rejection-maintained)** The rejection of Claims 1-16, 23, 54-60, 62, 63 and 65

under 35 USC 103(a) as being unpatentable over Vitiello (US 6,322,789) and Tam (PNAS

86:9084-9088, 1989), is maintained for the reason of record.

In response to Applicant's argument:

8. Tam teaches that the **preS2 peptide determinant serves as a T helper cell epitope**, but not as a B cell epitope (Emphasis added by Applicants). As such, a skilled artisan would have no motivation to add the preS2 peptide of SEQ ID NO: 48 taught by Tam to the polypeptide of Vitiello, because the polypeptide of Vitiello *already contains* a T helper cell epitope.

9. Applicant's argument is not convincing for following reasons: First, Applicants indicated that a peptide of SEQ ID NO: 48 (corresponding to preS region) represents "sequence 3... B cell epitope from HBV" (e.g. Claim 1); see last Para, p. 19, election of species, filed on July 6, 2009. Thus, Applicant has admitted on the record that a peptide of SEQ ID NO: 48 is a B cell epitope. The cited Tam reference teaches the structural limitation of sequence 3 elected by Applicant.

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More importantly, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In the present case, Tam teaches multiple antigen peptides (MAP) vaccine, in which HBV T and B cell epitopes are covalently linked together by linking peptides, see e.g. Abstract, and Fig. 1. Tam teaches that the MAP which contains both T and B epitopes can enhance immune responses and overcome the poor immunogenicity encountered with a single epitope. This teaching has taught and would motivate one of ordinary skill in the art to combine both T helper and B cell epitope cell in order to enhance immune responses and overcome the poor immunogenicity encountered with a single epitope. The cited Vitiello reference shows the peptides comprising both T helper and CTL epitopes were superior in inducing immune responses when injected into mice, see Example IV-VI. Vitiello also explicitly suggests include additional T helper epitopes from HBV or other antigens in a vaccine against HBV; see e.g. line 50, col. 3 to line 19, col. 4. In view of the combined teaching and the successful examples taught by Vitiello and Tam, one skilled in the art would have been motivated to generate the claimed immunogen comprising T-helper and CTL epitopes, as well as B cell epitopes. Applicant's argument is therefore not persuasive.

10. Applicant argues (2) that Tam teaches away from the claimed invention because Tam teaches that tetanus toxoid carrier is not suitable for use in human vaccines.

11. This argument is considered but not persuasive. First, neither Vitiello nor Tam use tetanus toxoid protein as a carrier. Vitiello uses a peptide of 14 amino acids from tetanus toxoid, not a tetanus toxoid protein. Thus Applicant's argument based on tetanus toxoid protein as a carrier is not relevant.

12. Applicant argues (3) that before the present application it was difficult to predict that the

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subject matter of Claim 1 would elicit strong immunity. For example, none of the cited references, whether alone or in combination, teach or suggest that an immunogen comprising a Th cell epitope, a CTM epitope from HBV, and a B cell epitope from HBV covalently linked together by linking peptides consisting of 3-7 amino acid residues would elicit strong immunity. As evidenced by the Examples 57 through 60, the claimed invention elicited stronger than expected immunity, and is not obvious under 35 USC 103(a).

13. Applicant's argument is considered but found not persuasive. The results shown by the specification are expected because they are consistent with the teachings and results shown by the cited prior art. Both Vitiello and Tam teach that combining multiple epitopes of T helper, B cell and/or B cell epitopes can enhance the immunogenicity of a peptide immunogen, and elicit stronger immune responses in a host. Therefore, the results shown by the specification are expected, and not surprising.

14. Since Applicant has not presented any compelling arguments, the rejection is maintained.

15. **(Prior rejection-maintained)** The rejection of Claims 64, 65, 71 and 72 under 35 USC 103(a) as being unpatentable over Vitiello (US6,322,789) and Tam (PNAS 86:9084-9088), as applied to Claims 1-16, 23, 54-60, 62, 63 and 65 above, further in view of Schneider (US 6,333,021), **is maintained** for the reason of record. Applicant has not presented any argument against this rejection.

16. **(Prior rejection-maintained)** The rejection of Claims 73 and 74 under 35 USC 103(a) as being unpatentable over Heathcote (Hepatology. 1999 Aug;30(2):531-536), in view of Tam (PNAS 86:9084-9088, 1989) and Vitiello (US6,322,789), **is maintained** for the reason of record. Applicant has not presented any argument against this rejection.

Remarks

17. No claim is allowed. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on Tu-F, 8:30-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/BO PENG/
Primary Examiner, Art Unit 1648